injury ~~disease~~ associated with the under production of collagen ~~as~~ in rheumatoid arthritis.

REMARKS

Amendments

Claims 1, 11, 15 and 16 have been amended for reasons of clarity and to overcome the 35 U.S.C. §112, second paragraph rejections. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**"

Status of the Claims

Claims 1, 3-4, 11-13, and 15-16 are pending herein. Claims 1, 11, 15 and 16 have been amended. Claims 5-10 and 17 have been cancelled as being drawn to a non-elected invention.

The 35 U.S.C. §112, second paragraph rejections

Claims 1, 3-4, 11-13 and 15-16 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The claim amendments clarify independent claims 1, 11 and 15, as helpfully suggested by the examiner. Dependent claims 3-4, 12-13 and 16 are clarified by the amendments to the corresponding independent claims. Accordingly, Applicants respectfully request that the

rejections of claims 1, 3-4, 11-13 and 15-16 under 35 U.S.C. §112, second paragraph, be withdrawn.

The 35 U.S.C. §103(a) rejection

Claims 1, 3-4, 11-13, and 15-16 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Pat. No. 4,711,780 (**Fahim**), U.S. Pat. No. 5,230,996 (**Rath**), **Saika** (abstract, 1993) or **Nowak** (abstract, 1997) alone or in combination, for the reasons set forth in Paper No. 7. This rejection is respectfully traversed.

Fahim teaches a medication for the topical treatment of epithelial tissue comprising vitamin C, a zinc salt and a sulfur amino acid. Only the combination of vitamin C, zinc salt and a sulfur amino acid is taught or suggested. There is no suggestion that vitamin C would be an effective treatment when used alone. The present invention, however, is drawn to a method of recovering cellular functions after injury by contacting the cells with ascorbic acid or a salt of ascorbic acid. The recovery of particular cellular functions as characterized by the present invention is also not taught or suggested by **Fahim**, so that **Fahim** does not teach or suggest the elements of the claims.

Rath teaches a solution of ascorbate and tranexamic acid for the treatment or prevention of cardiovascular disease. Ascorbate is taught for the purpose of reducing lipoprotein (a) in the

bloodstream, and tranexamic acid inhibits binding of lipoprotein (a) to the blood vessel walls. In contrast, the present application claims ascorbic acid or an ascorbic acid salt in a method to recover cellular functions following cell injury. **Rath** therefore does not teach or suggest the elements in the claimed methods.

Saika teaches a healing effect of ascorbic acid or ascorbic acid phosphate on alkali burns in the corneas of rabbits; the healing effects observed include an increase in non-burned stroma and basal lamina under new epithelia with treatment. The present invention describes the effects of ascorbic acid or an ascorbic acid salt on recovery of other cellular functions following injury, such as mitochondrial function, Na^+-K^+-ATPase protein expression and activity, and active Na^+ transport. These functions are not taught or suggested by **Saika**. In addition, the present invention discloses that the recovery of cellular functions by ascorbic acid or an ascorbic acid salt was accomplished by a mechanism distinct from the antioxidant activity of ascorbic acid; no such distinction is taught or suggested by **Saika**. Therefore, there is no teaching or suggestion present in **Saika** to combine the elements of the claimed invention.

Nowak (1997) teaches the stimulation of regeneration by ascorbic acid in tert-butylhydroperoxide-exposed renal cells. Treatment with ascorbic acid did not prevent cell injury, but promoted regeneration by stimulating proliferation and cell migration/spreading and decreasing cell death during the recovery

period. Exposure to tert-butylhydroperoxide in **Nowak** left the cells able to recover on their own without ascorbic acid treatment; however, exposure of renal cells to dichlorovinyl-L-cysteine in the present invention required ascorbic acid phosphate treatment to recover. This difference suggests that the ascorbic acid brought about recovery of cellular functioning in the present invention via a different mechanism than that taught by **Nowak**, characterized in the present invention by the restoration of specific cellular functions such as Na^+-K^+-ATPase expression and activity, mitochondrial function, and active Na^+ transport. These functions are not taught or suggested by **Nowak**.

Because the references cited do not teach or suggest the particular combination of elements claimed in the present invention, they do not render the present claims obvious. In addition, no combination of the claimed elements is taught or suggested by any combination of the cited references. Considering the invention as a whole, none of the cited references teaches the recovery of the particular cellular functions characterized and claimed in the present invention. Because these functions are not taught or contemplated by the prior art, there is no motivation for one skilled in the art to combine the elements of the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 1, 3-4, 11-13, and 15-16 under 35 U.S.C. §103(a) be withdrawn.

This is intended to be a complete response to the Final Office Action mailed November 5, 2002. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution. Should any additional fees be due, please debit Deposit Account 07-1185.

Respectfully submitted,

Date: April 7, 2003

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"VERSION WITH MARKINGS TO SHOW CHANGES MADE"

IN THE CLAIMS:

Please cancel claims 5-10 and 17 as being drawn to a nonelected invention.

Please amend claim 1 as follows:

1. (Twice amended) A method of recovering cellular functions *in vitro* in cells following injury, comprising the step of:

contacting said cells with ascorbic acid or a salt of ascorbic acid,

wherein said cellular functions ~~include~~ are selected from the group consisting of proliferation, mitochondrial function, Na^+-K^+-ATPase protein activity, and active Na^+ transport.

Please amend claim 11 as follows:

11. (Twice amended) A method of recovering cellular functions following injury in an individual in need of treatment, comprising the step of:

administering a therapeutically effective amount of ascorbic acid or a salt of ascorbic acid to said individual,

wherein said cellular functions ~~include~~ are selected from the group consisting of proliferation, mitochondrial function, Na^+-K^+-ATPase protein expression, Na^+-K^+-ATPase protein activity, and active Na^+ transport.

Please amend claim 15 as follows:

15. (Twice amended) A method of recovering cellular functions in an eye ~~diseases~~ disease or following an injury to the eye of an individual in need of treatment, comprising the step of:

administering an ophthalmic composition comprising a therapeutically effective amount of ascorbic acid or a salt of ascorbic acid in an ophthalmically acceptable carrier to said individual,

wherein said cellular functions ~~include~~ are selected from the group consisting of proliferation, mitochondrial function, Na^+-K^+-ATPase protein expression, Na^+-K^+-ATPase protein activity, and active Na^+ transport and wherein said ascorbic acid is in the concentration range of from about 0.05 mM to about 0.5 mM.

Please amend claim 16 as follows:

16. (Twice amended) The method of claim 15, wherein said injury is selected from the group consisting of acute injury to the eye, ~~eye diseases~~ eye injury associated with the over production of

collagen ~~as~~ in conjunctivitis ~~and~~ or diabetes mellitus, and eye injury ~~disease~~ associated with the under production of collagen ~~as~~ in rheumatoid arthritis.